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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,476	12/07/2001	Norbert O. Reich	G&C 30794.30-US-D1	8266

7590 09/09/2004

Attn: Karen S. Canady
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EXAMINER

MCINTOSH III, TRAVIS C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/010,476

Applicant(s)

REICH ET AL.

Examiner

Traviss C McIntosh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-30 and 32-35 is/are pending in the application.
- 4a) Of the above claim(s) 28-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-27 and 32-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Amendment filed June 23, 2004 has been received, entered into the record, and carefully considered. The status of the claims is as follows:

Claims 1-20 and 31 are canceled.

Claims 28-30 have been withdrawn.

Claims 21-27 and 32-35 are pending.

Remarks drawn to rejections of Office Action mailed February 23, 2004 include:

102 rejections: which have been maintained for reasons of record.

An action on the merits of claims 21-27 and 32-35 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

The rejection of claims 21, 24 and 33-35 under 35 U.S.C. 102 (e) as being anticipated by Sufrin et al. (US Patent 5,652,105) is maintained for reasons of record.

Claim 21 is drawn to a method of inhibiting the methylation of DNA comprising contacting a DCMTase with a synthetic inhibitor molecule in the presence of DNA wherein the inhibitor molecule comprises a C-5 methylcytosine molecule which binds to an allosteric site on the DCMTase, which inhibits the methyltransferase activity. Claim 24 provides that the inhibitor is an oligonucleotide comprising the C-5 methylcytosine molecule. Claim 33 provides that the

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subject is human, claim 34 provides the subject is an animal, and claim 35 provides the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine, or canine.

Sufrin et al. disclose an oligomeric DNA analog which comprises at least one 5-methylcytosine residue which specifically interacts with mammalian DCMTase (abstract). Moreover, Sufrin et al. disclose that their analogs are useful to inhibit DNA methyltransferase activity in tumor cells (column 3, lines 28-33). Sufrin et al. additionally disclose that their analogs appear to interact with both an activation and a catalytic site on the enzyme (column 7, lines 29-31). Moreover, Sufrin et al. disclose that their analogs were artificially constructed (column 4, lines 54-58). Sufrin et al. disclose that their analogs are effective in inhibiting DCMTase activity in humans (column 1, lines 42-53) as well as mice (column 2, lines 52-61).

The disclosure of Sufrin's 5-methylcytosine containing oligomeric DNA and their use of the same to inhibit mammalian DCMTase activity is seen to anticipate claims 21, 24, and 33-35 of the instant application.

The rejection of claims 22-23, 25-27, and 32 under 35 U.S.C. 102(e) as being anticipated by Sufrin et al. (US Patent 5,652,105) is maintained for reasons of record.

Claim 22 is drawn to a method of inhibiting the proliferation of cancer cells comprising administering a synthetic inhibitor molecule that comprises a C-5 methylcytosine molecule which binds to an allosteric site on the DCMTase, which inhibits the methyltransferase activity. Claim 23 provides that the cancer is from lung, breast, prostate, pancreas, or colon. Claim 25 provides that the subject is human, claim 26 provides the subject is an animal, and claim 27 provides the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine, or canine.

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Claim 32 provides that the inhibitor is an oligonucleotide comprising the C-5 methylcytosine molecule.

Sufrin et al. disclose an oligomeric DNA analog which comprises at least one 5-methylcytosine residue which specifically interacts with mammalian DCMTase (abstract). Moreover, Sufrin et al. disclose that their analogs are useful to inhibit DNA methyltransferase activity in tumor cells (column 3, lines 28-33). Sufrin et al. additionally disclose that their analogs appear to interact with both an activation and a catalytic site on the enzyme (column 7, lines 29-31). Moreover, Sufrin et al. disclose that their analogs were artificially constructed (column 4, lines 54-58). Sufrin et al. disclose that their analogs are effective in inhibiting DCMTase activity in humans (column 1, lines 42-53) as well as mice (column 2, lines 52-61). Moreover, Sufrin disclose that lowering the level and activity of DCMTase also lowers the incidence of colon cancer (column 2, lines 52-61).

The disclosure of Sufrin's 5-methylcytosine containing oligomeric DNA and their use of the same to inhibit mammalian DCMTase activity and the disclosure of inhibiting DCMTase activity in decreasing methylation which lowers incidence of cancer is seen to anticipate claims 22-23, 25-27, and 32 of the instant application.

Applicant's arguments filed June 23, 2004 have been fully considered but they are not persuasive. Applicants argue that prior to their invention, those skilled in the art did not know that DCMTase is regulated via an allosteric site, nor that such allosteric inhibition could be achieved using a synthetic inhibitor molecule which comprises a C-5 methylcytosine. However, the examiner would like to note that Sufrin et al.'s methodological step of administering their 5-

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methycytosine containing oligomeric DNA would have inherently performed the method as instantly claimed. It is noted that if Sufrin et al., having taken the manipulative steps described therein, had attempted to measure for the results as described in the instant application, Sufrin would have uncovered those results, as they are directly correlative to the method as practiced by Sufrin. Applicant's discovery of differing effects of a prior art method does not give the discoverer a right to exclude others from practicing the prior arts method of using 5-methycytosine containing products to inhibit the activity of DCMTase, as the prior arts method would have inherently performed the method as instantly claimed. See *Ex Parte Novitski*, 26 *USPQ 2d (BNA) 1389*. A hypothetical example clarifies this principle. Humans lit fires for thousands of years before realizing that oxygen is necessary to create and maintain a flame. The first person to discover the necessity of oxygen certainly could not have obtained a valid patent claim for "a method of making a fire by lighting a flame in the presence of oxygen." Even if prior art on lighting fires did not disclose the importance of oxygen and one of ordinary skill in the art did not know about the importance of oxygen, understanding this law of nature would not give the discoverer a right to exclude others from practicing the prior art of making fires. *EMI v. Cypress Semiconductor*, 2001 US Fed. Cir. Ct. of App. In the instant case, applicant's arguments that Sufrin et al. did not know that inhibition is via an allosteric site are not found to be convincing.

Applicants additionally argue that Sufrin et al. does not demonstrate that the differences in enzyme activity are attributed to inhibition or activation. However, Sufrin et al. is taken for what it teaches in it's entirety, and that is inhibiting DCMTase with a 5-methycytosine containing moiety (see claims 18 and 19 for example). Moreover, applicants argue that Sufrin et

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al. does not indicate that their inhibition was caused by another molecule or resulted from substrate inhibition, or that they distinguished between competitive and allosteric inhibition. However, as set forth supra, Sufrin et al. clearly teach that 5-methylcytosine containing moieties inhibit DCMTase activity.

Applicants additionally argue that their claims require (a) inhibiting methylation of DNA comprising (b) contacting DCMTase with a synthetic inhibitor molecule (c) so as to form an enzyme / synthetic inhibitor molecule complex in the presence of DNA wherein (d) the inhibitor molecule comprises a C-5 methylcytosine molecule which (e) binds to an allosteric site on the DCMTase which inhibits methyltransferase activity. Applicants then state that the Patent Office has not shown that all of these elements are met by the cited reference and that Sufrin fails to teach (a) inhibition as it is understood by those skilled in the art, (c) formation of an enzyme / synthetic inhibitor complex in the presence of DNA, or (e) binding to an allosteric site on the DCMTase. Thus, applicants admit that Sufrin et al. teach steps (b), contacting DCMTase with a synthetic inhibitor molecule, and (d), that the inhibitor molecule comprises a C-5 methylcytosine molecule. Thus, the method of Sufrin et al. must have inherently performed the steps as instantly claimed as the same active agent is known to inhibit the same enzyme. Moreover, applicants argue that Sufrin et al. is silent to the contacting the enzyme with the inhibitor in the presence of DNA. However, the examiner notes that the enzyme DCMTase is known to methylate DNA, thus the inhibition of the enzymes activity as taught by Sufrin et al. must have been performed in the presence of DNA, as DNA is what DCMTase acts upon, and thus inhibiting the activity of the enzyme as taught by Sufrin et al. would necessarily require DNA to be present to determine

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if the enzyme did or did not subsequently methylate the DNA in the presence of their 5-methylcytosine containing moieties.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

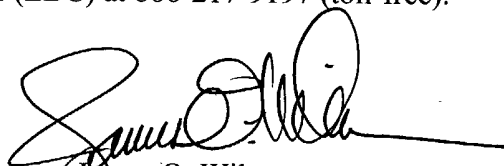
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
August 31, 2004



James O. Wilson
Supervisory Patent Examiner
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